UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
[illegible]	[illegible]/96	HARRISON	10305

HM11/0221

SCULLY SCOTT MURPHY & PRESSER
400 GARDEN CITY PLAZA
GARDEN CITY NY 11530

EXAMINER	
VANDER VEGT,P	

ART UNIT	PAPER NUMBER
1644	25

DATE MAILED: 02/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
08/663,272	Harrison et al
Examiner	**Group Art Unit**
F. Pierre VanderVegt	1644

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), ~~or thirty days, whichever is longer,~~ from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *39, 40, 42, and 43* ~~is~~/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *39, 40, 42, and 43* ~~is~~/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

This application is a 371 of PCT/AU96/00085.

Claims 39, 40, 42 and 43 are currently pending in this application.

1. Applicant is advised that the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2000 were published subsequent to the prior Office Action and the claims have been examined in view of these guidelines. The following rejection is set forth herein.

2. **THIS OFFICE ACTION IS NON-FINAL.**

Claim Rejections - 35 USC § 112

3. Claims 39, 40, 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth peptides of the formula $X_1X_2X_3$ of 10-45 amino acid residues of GAD65, with the core sequence contiguous within amino acids 506-518, or proinsulin, with the core sequence contiguous within amino acids 24-36. The written description is not commensurate in scope with the claims drawn to "homologous" sequences [claims 39 and 42], "derivatives" [39, 40, 42 and 43] or "chemical equivalents" [40, 43] of the disclosed GAD65 or proinsulin sequences.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification

does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

With the exception of SEQ ID NO:1 and SEQ ID NO:2, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide molecules and therefore conception is not achieved, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,((CAFC, 1991) 18 USPQ2d 1016).

The instant specification defines "derivatives" at page 4, lines 20-26, as including "any single or multiple amino acid substitution, deletion and/or addition relative to the naturally occurring amino acid sequence in the native molecule from which the peptide is derived including any single or multiple substitution, deletion and/or addition of other molecules associated with the peptide, including carbohydrate, lipid and/or other proteinaceous moieties. Such derivatives, therefore, include glycosylated or non-glycosylated forms or molecules with altered glycosylation patterns." The instant specification fails to define the meaning of the terms "homologous" and "chemical equivalent" relative to the claimed invention. Percent sequence homology is not defined in the claim nor does it appear to be defined in the disclosure. Further, "homologous" is an evolutionary term which does not indicate any degree of sequence similarity or identity.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* ((CAFC, 1997) 43 USPQ2d 1398), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a

DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention." It is respectfully submitted that the facts in the instant application, while drawn to peptides, read upon the situation in *U of C v. Lilly,* drawn to nucleic acids, because the instant specification does not recite a representative number of peptides, defined by an amino acid sequence, in order to define what falls within the scope of the claimed genera of claims 39, 40, 42 and 43 were in Applicant's possession at the time of filing. This is insufficient to support the scope of the claims as provided by the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement published in the January 5, 2000 Federal Register at Volume 66, No. 4, pages 1099-1111.

Therefore only polypeptides of GAD65 and proinsulin comprising the disclosed species of SEQ ID NO:1 or SEQ ID NO:2, but not the full breadth of "homologous" sequences, "chemical equivalents" or "derivatives" of the sequences meets the written description provision of 35 USC 112, first paragraph.

4. Claims 39, 40, 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for peptide sequences from GAD65 or proinsulin comprising SEQ ID NO:1 or SEQ ID NO:2, does not reasonably provide enablement for homologous sequences, derivatives, chemical equivalents or non-naturally occurring amino acid residues. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Briefly, the claims are drawn to polypeptides of the formula $X_1X_2X_3$ of 10-45 amino acid residues of GAD65, with the core sequence contiguous within SEQ ID NO:1, or proinsulin, with the core sequence contiguous within SEQ ID NO:2. The claims encompass not only polypeptides derived directly from the amino acid sequence of the native protein, but also recite homologues of the sequences, derivatives and chemical equivalents thereof. The claims further recite the inclusion of "non-naturally occurring" amino acid residues. The instant specification is not enabling for the species of the claim which are not drawn to polypeptides consisting of naturally

occurring contiguous sequences from proinsulin or GAD comprising the recited core sequences. The instant specification does not disclose what Applicant regards as a "non-naturally occurring" amino acid residue in the context of the instant invention. The term could alternatively mean one of the 20 known natural amino acids which does not naturally occur in a particular position within the native sequence of the protein or the term could mean that attached to the amino acid backbone portion of the molecule is a side group not found in nature or one that has been chemically altered. Further , the term "chemical derivative" also could mean an altered side-chain or it could mean alterations of the amino acid backbone. The specification fails to provide any disclosure regarding the meaning of the terms and also fails to provide any guidance on how to make the compound for the practice of the claimed method. The practice of the claimed method of claims 42 and 43 requires the administration to a subject of a substance which is effective for the removal or reduction of autoreactive T cells from said subject. The practitioner is not provided with any guidance regarding the manufacture of homologous sequences or sequences comprising derivatives, chemical equivalents or non-naturally occurring amino acid residues. Based upon the paucity of guidance, the artisan would not be able to predict compounds which would be effective in the claimed method. Besides the specific peptide sequences from GAD65 or proinsulin comprising SEQ ID NO:1 or SEQ ID NO:2 disclosed in the specification, the specification fails to provide any guidance as to how to determine the active amino acid residues of the peptide compound. Since the amino acid sequence of a peptide determines its structural, immunogenic and functional properties, predictability of which changes can be tolerated in a peptide's amino acid sequence and still retain similar immunogenicity and functionality requires a knowledge of and guidance with regard to which amino acids in the peptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a protein's structure relates to its immunogenic determinants and functional usefulness. However, the problem of predicting peptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain immunological and functional aspects of putative GAD65 or proinsulin homologue and finally what changes can be tolerated with respect thereto is complex

and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to make and practice the claimed invention and this is not sanctioned by the statute.

Conclusion

5. No claim is allowed.

6. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2001 365-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
February 21, 2001

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1640